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**WO 01/89518 A1**

(54) Title: METHOD OF DETERMINING A DOSAGE OF ANTI-OXIDANT FOR AN INDIVIDUAL

(57) Abstract: A method of determining a dosage of anti-oxidant for an individual person, wherein the dosage is determined on the basis of an individual factor and a stress index. The individual factor is based on a weight factor of the individual, an age factor of the individual and a training factor of the individual. The training factor is based on training history of the individual, and the stress index is based on current and/or future physical activity of the individual. The invention also comprises an anti-oxidant mixture comprising bioflavonoids from pine bark, alpha lipoic acid, Vitamin C and Vitamin E.

## METHOD OF DETERMINING A DOSAGE OF ANTI-OXIDANT FOR AN INDIVIDUAL

This invention relates to a method of determining a dosage of anti-oxidant for an individual person and more particularly, but not exclusively, to a method of determining a dosage of anti-oxidant for an athlete.

Molecular oxygen is essential in the production of energy that our bodies need in order to perform aerobic exercise. This process, which occurs within the mitochondria of the cell, involves oxygen accepting up to four additional electrons, and is called an oxidation reaction. However, when molecular oxygen only accepts between one and three electrons, a variety of oxygen free radicals (called superoxide, peroxide or hydroxy radicals) are formed, which because oxygen is only partly oxidised, and these are extremely reactive owing to oxygen being only partly oxidised. It is estimated that for every 100 oxygen molecules involved in oxidative metabolism, approximately four of them form oxygen radicals.

Anti-oxidants are chemical molecules, present in small amounts in the body that can accept an electron from an oxygen radical, thus deactivating it, and preventing oxidative damage. The body produces its own anti-oxidants, the most important of which is glutathione or GSH. The body also produces four anti-oxidant enzymes (superoxide dismutase, catalase, glutathione peroxidase and glutathione reductase), which can detoxify the oxygen radicals to harmless molecules such as water. These anti-oxidant enzymes require the mineral cofactors, selenium, copper, zinc, iron and manganese to function effectively. Selenium is of particular importance in some parts of the world as many of the soils are selenium deficient.

Vitamins E, C and A have long been recognised as important anti-oxidants obtained from our diet. In addition, a diverse group of compounds called flavonoids are found in many plants, fruits and vegetables. Flavonoids including oligomeric proanthocyanidins (OPC's) are now recognised as a key source of dietary anti-oxidants and

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play an important role in human health. Particularly high concentrations of flavonoids and OPC's are found in the bark of *Pinus radiata* trees. Bioflavonoids are extracted from the bark of young New Zealand *radiata* pine trees using only pure water in a water extraction process. Such bioflavonoids are a potent source of OPC's and other important natural dietary anti-oxidants. Another anti-oxidant, alpha lipoic acid, has recently been found to increase the levels of GSH inside the cell, thus increasing the body's protection against oxidative damage.

When the number of oxygen free radicals within the body increases beyond the amount of anti-oxidants in the body, the body is said to be under "oxidative stress". These oxygen radicals rapidly react with fats, proteins and DNA, damaging their molecular structure, which can cause abnormal metabolic and cellular functions, disruptions in cell structure, leakage of essential enzymes involved in energy production and genetic damage that may lead to the development of chronic diseases, such as cancer, later in life.

Intense exercise increases aerobic metabolism (and hence oxygen radical production) by up to 20 times compared with normal resting conditions. This means that the level of oxidative stress experienced by the body is increased in proportion to the exercise intensity. The blood levels of GSH rapidly decrease in response to moderate intensity exercise, and as a consequence oxidative damage increases. Recent research has shown that the use of high-potency anti-oxidant supplements can significantly reduce measures of muscle, blood cell and tissue damage in athletes and active individuals by at least 25%. An increase in the total anti-oxidant capacity resulting from regular physical activity may also be responsible for the reduced muscle fatigue and improvements in physical performance. It has recently been suggested that all active individuals should take anti-oxidant supplements to reduce the likelihood of developing many diseases shown to be associated with oxidative degeneration.

As recovery from exercise is a major concern for athletes in heavy training, a reduction in the level of tissue damage means a faster recovery for the athlete. In addition, research has also shown that anti-oxidant supplements increase the plasma testosterone to

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cortisol ratio during the post-exercise recovery period, thus assisting muscle repair regeneration.

5 The important role that dietary anti-oxidants can play on the health and performance of athletes is only now becoming recognised. Anti-oxidants have been shown to reduce muscle and tissue damage and to help prevent the onset of degenerative diseases.

Anti-oxidants can also play a role in improving the health, fitness and well-being of people living in the modern, high-stressed, fast-paced world.

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However, the dosage of anti-oxidants is typically haphazard, and it would be beneficial for there to be a systematic method of determining a dosage of anti-oxidants according to the body's requirements.

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In accordance with one aspect of the present invention, there is provided a method of determining a dosage of anti-oxidant for an individual person, wherein the dosage is determined on the basis of an individual factor and a stress index, the individual factor being based on a weight factor of the individual, an age factor of the individual and a training factor of the individual based on training history of the individual, and the stress

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In accordance with another aspect of the present invention, there is provided a method of determining a dosage of anti-oxidant for an individual person, wherein the dosage is determined on the basis of an individual factor (IF) and a stress index (SI),

25

$$IF = WF + AF + TF,$$

SI = Sum of {PATF  $\times$  TIF  $\times$  TTF} for each possible PATF/TIF combination,  
and the dosage increases as each of IF and SI increases;

wherein

WF is the weight factor which increases with increasing weight of the individual,

30

AF is the age factor which increases with increasing age of the individual,

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TF is the training factor which increases as the extent of past physical training of the individual decreases,

PATF is a physical activity type factor of a current and/or future physical activity of the individual and PATF increases as the physical exertion required to perform the corresponding physical activity increases,

TIF is the training intensity factor, where TIF increases as the intensity of the individual's performance of a corresponding physical activity increases, and

TTF is a training time factor for a corresponding PATF/TIF combination, where TTF increases as the time spent by the individual performing a corresponding physical activity increases.

In accordance with another aspect of the present invention, there is provided an anti-oxidant mixture comprising the following amounts of the following constituents: between 100c and 200c mg of bioflavonoids extracted from pine bark extract, between 50c and 100c mg of Alpha lipoic acid, between 50c and 100c mg of Vitamin C and/or its derivatives, and between 100c and 200c mg of Vitamin E and/or its derivatives, wherein c is a positive number.

The invention will now be further described with reference to more detailed examples.

The applicant has determined that the type, intensity, duration and frequency of an individual's training determines the individual's level of oxidative stress, and thus his or her oxidative stress index (OSI). The greater the OSI, the greater the dose of anti-oxidant required to detoxify the oxygen radicals generated. In addition, factors such as age, weight, gender and whether the individual is trained or untrained will determine his or her body's individual anti-oxidant capacity.

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a) **Exercise type**

Since oxygen radicals are produced as a by-product of aerobic metabolism, strenuous aerobic exercise requires a greater level of anti-oxidant protection than does  
5 exercise that relies more on anaerobic metabolism, muscular strength and power. Many field and court sports such as rugby or tennis are a combination of aerobic and anaerobic energy production, and still require anti-oxidant supplementation. Studies have shown significantly lower plasma vitamin E and C levels in elite swimmers compared to basketballers and gymnasts, which is indicative of the higher level of oxidative stress in  
10 endurance athlete groups.

b) **Exercise intensity**

15 The higher the exercise intensity, especially during aerobic exercise, the greater the oxygen consumption, which means higher levels of oxidative stress are placed on the active tissues of the body. Research has demonstrated that increased exercise intensity results in greater levels of oxidative stress and damage.

20

c) **Exercise duration and training frequency**

The longer the exercise duration and the greater the training frequency, the greater the numbers of oxygen radicals produced within the body. Increased training volumes,  
25 particularly in those sports that are aerobically based, have been shown to cause depletion of plasma and tissue anti-oxidants.

d) **Age and gender**

30

As we age, our anti-oxidant capacity and hence our ability to cope with increasing

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levels of oxidative stress declines. The levels of plasma GSH progressively decrease from 25 to 45 years of age to 50% of their original level, irrespective of the state of training. As a consequence the concentration of lipid peroxides, an index of oxidative damage to lipids, rises with increased age.

5

In addition, the capacity of the anti-oxidant enzymes has been shown to decrease with increasing age. This means that there is an increased need for supplemental anti-oxidant protection as we age, especially when undertaking strenuous exercise.

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The female sex hormone, oestrogen, has been shown to possess anti-oxidant activity, so women in their reproductive years [ie. prior to menopause at around 50 years], have a lower requirement for exogenous anti-oxidants than men of similar age. In other words, females of similar age tend to have lower levels of oxidative damage than males. However, after menopause, women have similar anti-oxidant requirements to men.

15

**e) Body weight**

Individuals with greater body [and muscle] mass need a proportionally greater dosage of anti-oxidant. This ensures that all metabolically active tissues are provided with adequate levels of anti-oxidant protection.

20

**f) Training level**

25

As athletes undertake training to increase their aerobic capacity, the capacity of their anti-oxidant enzyme systems also increases. Consequently the ability to protect their metabolically active tissues against the oxidative stress produced during training is increased. As the irregularly active individual does not achieve these adaptations, the use of anti-oxidant supplements is probably even more important for untrained individuals. Despite these enzymatic adaptations, the level of residual oxidative damage is still present

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in trained athletes at rest.

Elite endurance athletes undertaking periods of heavy training have an increased susceptibility to "overtraining". This syndrome is characterised by impaired physical  
5 performance, prolonged periods of fatigue, increased levels of muscle damage and soreness, hormonal disturbances and impaired immune function. Anti-oxidant supplementation has been shown to significantly reverse a hormonal indicator of overtraining, enhance immune function and reduce the frequency of infective episodes following exercise. The anti-inflammatory properties of anti-oxidants may also reduce  
10 chronic muscle soreness associated with heavy training.

The applicant has determined a method of determining a dosage of anti-oxidant for an individual, based on the above factors. A preferred embodiment of the invention will now be described, by way of example only, with reference to the tables and equations  
15 incorporated herein.

In accordance with a preferred embodiment of the present invention, there is provided a method of determining a dosage of anti-oxidant for an individual person, including the following steps.

20

#### **Step 1: Determine an Individual Factor (IF)**

To determine the individual factor based on an individual's age, gender and body  
25 weight, the following equation is used:

$$\text{Individual Factor (IF)} = \text{Age Factor} + \text{Weight Factor} + \text{Training Factor},$$

where the Age Factor, Weight Factor and Training Factor are determined as follows.

30



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## (i) Age Factor (AF)

Male	less than or equal to 30 years	31 to 45 years	greater than or equal to 45 years
Female	less than or equal to 35 years	36 to 55 years	greater than or equal to 55 years
Age Factor	1	1.5	2

TABLE 1

5

## (ii) Body Weight Factor (WF)

Weight	less than or equal to 60kg	60kg to 90kg	greater than or equal to 90kg
Weight Factor	1	1.25	1.5

TABLE 2

10

## (iii) Training Factor (TF)

Whether the individual is "trained" or "untrained" has an important bearing on the capacity of the individual's anti-oxidant enzymes to detoxify oxygen free radicals.

15

The following guidelines are provided to determine whether the individual is classified as "trained" or "untrained".

If, over the past 3 months, the individual has been exercising aerobically at least 5 times per week for at least 30 minutes at a moderate intensity level, the individual is considered to be "trained". Alternatively, other tests may be used, for example, if the individual raises a significant sweat response in mild conditions (20 - 25°C), he or she may be considered "trained".

20

If the individual is "trained", he or she has a Training Factor of 0. If the individual is "untrained", the individual has a Training Factor of 0.5.

It is now possible to calculate the Individual Factor of the individual by adding

25

together the Age Factor, the Body Weight Factor, and the Training Factor.

### Example

5

$$\text{Individual Factor (IF)} = \text{Age Factor} + \text{Weight Factor} + \text{Training Factor}$$

As an example, consider a case in which the individual is an untrained male, 40 years of age, with a body weight of 85kg.

10

The Individual Factor of the individual is calculated as:

$$\text{IF} = 1.5 + 1.25 + 0.5 = 3.25,$$

15 where the components added are determined by sections (i) to (iii), above.

### Step 2: Determine the Oxidative Stress Index (OSI)

20

The type, intensity, duration and frequency of the individual's training determines his or her level of oxidative stress. The OSI is based on the individual's training load and is determined by the following equation:

$$\text{OSI} = \frac{\text{Sum} \{ \text{Physical Activity Type Factor (PATF)} \times \text{Exercise Load Factor (ELF)} \}}{10},$$

25

where 10 is an arbitrary scaling factor to get the OSI values within a desired range to facilitate presentation in a convenient form (see for example Table 8, below).

Calculation tables such as those in Tables 5 to 7 may be provided to assist in  
30 performing this calculation.

(i) **Physical Activity Type Factor (PATF)**

- 5 Consider the main physical activities of the individual (either while training or competing) and allocate a "physical activity type factor" (ie. a number from 1 to 3) from Table 3, below, for each physical activity type. Different activities may be written into tables, such as those in Tables 5 to 7, in order of the "physical activity type factor".

Physical Activity Classification	Physical Activity Type Factor	Typical Physical Activities
Heavy endurance sports		3 Triathlon and ultra-endurance sports, distance and cross-country running, swimming, road cycling, cross-country skiing, rowing and paddling
Combination aerobic & anaerobic sports, field games & court sports, combat sports		2 Alpine skiing, track cycling, ice-skating, soccer, rugby, touch rugby, Australian rules football, basketball, squash, tennis, badminton, table tennis, boxing, wrestling, judo
10 Low intensity aerobic strength & power, sports skills, target and artistic sports		1 Golf, fencing, sprinting and field sports in track and field, anaerobic sports, weight training and weight lifting, bodybuilding, gymnastics, diving, shooting, archery

TABLE 3

15 (ii) **Exercise Load Factor (ELF)**

To determine the exercise load factor of the individual for each physical activity type, the following formula may be used, and is based on the various training types and the number of hours spent at each during a typical training week.

20

$$\text{Exercise Load Factor} = \{\text{Training hours per week (TTF)} \times \text{Training Intensity Factor (TIF)}\}$$

The training intensity for each training type is estimated and is assigned a Training

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Intensity Factor as follows. The number of hours spent by the individual doing each physical activity each week is also estimated. These values are entered into tables, such as those in Tables 5 to 7.

	Training Intensity Factor
Easy or low intensity	1
Moderately hard training or moderate intensity training	2
Hard, high intensity or near maximal training	3

TABLE 4

**Example:**

- 10 Consider the case in which the individual is a distance runner ( $IF = 3.25$ ) who completes an average of 12 hours in total per week, (average of 2 hours of training per day, 6 days per week), the 12 hours being spent as follows: 3 hours per week Race/Pace and Hill Training at a moderate intensity; 6 hours per week Slow Distance running at a low intensity; and 3 hours per week Interval Training at near maximum intensity. The individual also performs moderate intensity weight training in two sessions per week for one hour per session. The OSI would be calculated as follows:

PATF 1 Activities	Weight training at near moderate intensity	OSI <sub>1</sub>
Intensity Factor	2	
Hours spent per week	2	
ELF (Intensity factor x hours)	4	
	$1 \times ELF = 1 \times 4$	4

TABLE 5

20

PATF 2 Activities	The individual performs no PATF 2 Activities	OSI <sub>2</sub>
Intensity Factor	0	
Hours spent per week	0	
ELF (Intensity factor x hours)	0	
	$2 \times ELF = 2 \times 0$	0

TABLE 6

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PATF 3 Activities	Race/pace and hill training	Slow distance running	Interval training at near maximum intensity	OSI <sub>3</sub>
Intensity Factor	2	1	3	
Hours spent per week	3	6	3	
ELF (Intensity factor x hours)	6	6	9	
	3 x ELF = 3 x (6+6+9) = 3 x 21			63

TABLE 7

$$5 \quad OSI = \frac{\text{Sum} \{ \text{Physical Activity Type Factor (PATF)} \times \text{Exercise Load Factor (ELF)} \}}{10}$$

=&gt;

$$10 \quad OSI = \frac{OSI_1 + OSI_2 + OSI_3}{10}$$

=&gt;

$$15 \quad OSI = \frac{4 + 0 + 63}{10} = \frac{67}{10} = 6.7$$

15 **Step 3: Determine the dosage of anti-oxidant using the Individual Factor (IF) and the Oxidative Stress Factor (OSI)**

20 Using the Individual Factor (IF) of the individual and the Oxidative Stress Factor (OSI) of the individual, the dosage of anti-oxidant for the individual can be determined by using the nomogram shown in Table 8, below.

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OSI Rating		Number of capsules of anti-oxidant per day								
Extreme	10	3	3	3	3					
Extreme	9	3	3	3	3	3				
Very heavy	8	2	3	3	3	3	3			
Very heavy	7	2	2	3	3	3	3	3		
Heavy	6	2	2	2	3	3	3	3	3	
Heavy	5	2	2	2	2	3	3	3	3	3
Moderate	4	1	2	2	2	2	3	3	3	3
Moderate	3	1	1	2	2	2	2	3	3	3
Light	2	1	1	1	2	2	2	2	3	3
Light	1	1	1	1	1	2	2	2	2	3
Individual Factor		2.00	2.25	2.50	2.75	3.00	3.25	3.50	3.75	4.00

TABLE 8

As an example of a dosage calculation, consider an individual with an IF of 3.25 and an OSI of 6.7. By finding the dosage in the nomogram corresponding to these IF and OSI values, it can be determined that the dosage of anti-oxidant for the individual is 3 capsules per day.

Numbers inside the nomogram represent the number of capsules per day recommended to be taken of an anti-oxidant, where each capsule comprises the following amounts of the respective constituents:

- 150mg of bioflavonoids extracted from pine bark extract;
- 50mg of Alpha lipoic acid;
- 100mg of a Vitamin C ester; and
- 150mg of Vitamin E as d-alpha – tocopherol acid succinate.

It should be noted that in place of or in addition to the above Vitamin C ester, each capsule may contain Vitamin C and/or its derivatives, for example sodium, calcium, magnesium and potassium salts of Vitamin C and Vitamin C esters.

It should also be noted that in place of or in addition to the above Vitamin E as d-alpha – tocopherol acid succinate, each capsule may contain Vitamin E and/or its derivatives, for example d-alpha tocopheryl acid succinate and d-alpha tocopheryl acid acetate.

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It is recommended that:

- when taking 3 capsules per day, one capsule is taken with water 10 to 20 minutes before each meal;
- 5 - when taking 2 capsules per day, one capsule is taken with water 10 to 20 minutes before morning and evening meals; and
- when taking 1 capsule per day, the one capsule is taken with water 10 to 20 minutes before the morning meal.

- 10       The preferred embodiment has been described by way of example only and modifications are possible within the scope of the invention.

Throughout this specification and the claims which follow, unless the context requires otherwise, the word "comprise", or variations such as "comprises" or  
15 "comprising", will be understood to imply the inclusion of a stated step or integer or group of steps or integers but not the exclusion of any other step or integer or group of steps or integers.

The reference to any prior art in this specification is not, and should not be taken  
20 as, an acknowledgment or any form of suggestion that that prior art forms part of the common general knowledge.

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THE CLAIMS DEFINING THE INVENTION ARE AS FOLLOWS:-

1. A method of determining a dosage of anti-oxidant for an individual person, wherein the dosage is determined on the basis of an individual factor and a stress index, the individual factor being based on a weight factor of the individual, an age factor of the individual and a training factor of the individual based on training history of the individual, and the stress index being based on current and/or future physical activity of the individual.
2. A method according to claim 1, wherein the weight factor increases with increasing weight of the individual, the age factor increases with increasing age of the individual, the training factor increases as the extent of past physical training of the individual decreases, the individual factor increases as each of the weight factor, the age factor and the training factor increases, the stress index increases as the extent of current and/or future physical activity increases, and the dosage increases as each of the individual factor and the stress index increases.
3. A method according to either claim 1 or claim 2, wherein the individual factor is the sum of the age factor, the weight factor, and the training factor.
4. A method according to any one of claims 1 to 3, wherein the stress index is based on a physical activity type factor, a training intensity factor and a training time factor.
5. A method according to claim 4, wherein the physical activity type factor of a physical activity increases as the physical exertion required to perform the physical activity increases, the training intensity factor increases as the intensity of the individual's performance of a physical activity increases, and the training time factor increases as the time spent by the individual performing a physical activity increases, and wherein the stress index increases as each of the physical activity type factor, the training intensity factor and the training time factor increases.



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6. A method according to claim 5, wherein the stress index is determined by multiplying together the physical activity type factor, the training intensity factor and the training time factor.
- 5
7. A method according to claim 6, wherein when the individual performs two or more physical activity types and/or performs a physical activity type at two or more intensities, the stress index is determined by multiplying together the corresponding physical activity type factor, training intensity factor and training time factor for
- 10 each physical activity type/training intensity combination to obtain a multiplied result, and by then adding together the multiplied results to obtain a total.
8. A method according to any one of claims 1 to 7, wherein the age factor is  $x$  if the individual is male and is less than or equal to 30 years of age or if the individual is
- 15 female and is less than or equal to 35 years of age, the age factor is  $2x$  if the individual is male and is greater than or equal to 45 years of age or if the individual is female and is greater than or equal to 55 years of age, and wherein the age factor is  $1.5x$  otherwise,  $x$  being a number.
- 20 9. A method according to any one of claims 1 to 5, wherein the body weight factor is  $y$  if the individual is less than 60 kilograms in weight, the body weight factor is  $1.5y$  if the individual is greater than 90 kilograms in weight, and wherein the body weight factor is  $1.25y$  otherwise,  $y$  being a number.
- 25 10. A method according to any one of claims 1 to 6, wherein the training factor is zero if in the 3 months immediately prior to performing the method the individual has exercised aerobically at least 5 times per week for at least 30 minutes each time, at a moderate intensity level, and wherein the training factor is  $0.5z$  otherwise,  $z$  being a number.

11. A method according to claim 4 or any one of claims 5 to 10 when dependent on claim 4, wherein a first set of physical activity types are assigned a physical activity type factor of  $a$  corresponding to a relatively low level of physical exertion required to perform the physical activity types of the set, a second set of physical activity types are assigned a physical activity type factor of  $2a$  corresponding to a relatively moderate level of physical exertion required to perform the physical activity types of the set, and a third set of physical activity types are assigned a physical activity type factor of  $3a$  corresponding to a relatively high level of physical exertion required to perform the physical activity types of the set,  $a$  being a number.
12. A method according to claim 4, or any one of claims 5 to 11 when dependent on claim 4, wherein the training time factor for a particular physical activity type/training intensity combination is the number of hours the individual spends per week performing the particular physical activity/training intensity combination.
13. A method according to claim 4, or any one of claims 5 to 12 when dependent on claim 4, wherein the training intensity factor for a particular physical activity type/training intensity combination is  $b$  if the individual performs the physical activity corresponding to said particular physical activity type/training intensity combination at an easy or low intensity, the training intensity factor for a particular physical activity type/training intensity combination is  $2b$  if the individual performs the physical activity corresponding to said particular physical activity type/training intensity combination at a moderately hard training or moderate intensity training level, and wherein the training intensity factor for a particular physical activity type/training intensity combination is  $3b$  if the individual performs the physical activity corresponding to said particular physical activity type/training intensity combination at a hard, high intensity or near maximal training level,  $b$  being a number.

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14. A method according to any one of claims 1 to 13, wherein the dosage of antioxidant for the individual is calculated by using the individual factor and the stress index to obtain a corresponding dosage from a nomogram.
- 5 15. A method according to any one of claims 1 to 14, wherein the dosage is in the form of a number of capsules to be taken by the individual per day.
16. A method according to either claim 14 or claim 15, when dependent on claims 8 to 11 and 13, wherein  $10a = b = x = y = z$ , and the nomogram is that shown in Table 8.
- 10 17. A method according to claim 16, wherein  $10a = b = x = y = z = 1$ .
18. A method according to any one of claims 15 to 17 when dependent on claim 15, wherein each capsule comprises between 100c and 200c mg of bioflavonoids from  
15 pine bark, between 50c and 100c mg of Alpha lipoic acid, between 50c and 100c mg of Vitamin C and/or its derivatives, and between 100c and 200c mg of Vitamin E and/or its derivatives, wherein c is a positive number.
19. A method according to claim 18, wherein each capsule comprises 150c mg of  
20 bioflavonoids from pine bark, 100c mg of Alpha lipoic acid, 100c mg of a Vitamin C ester, and 100c mg of Vitamin E as d-alpha - tocopherol acid succinate, wherein c is a positive number.
20. A method according to claim 18, wherein each capsule comprises 150c mg of  
25 bioflavonoids from pine bark, 50c mg of Alpha lipoic acid, 100c mg of a Vitamin C ester, and 150c mg of Vitamin E as d-alpha - tocopherol acid succinate, wherein c is a positive number.
21. A method according to any one of claims 18 to 20, wherein  $c = 1$ .

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22. A method of determining a dosage of anti-oxidant for an individual, substantially as hereinbefore described with reference to Tables 1 to 8.
23. A method of determining a dosage of anti-oxidant for an individual person, wherein  
5 the dosage is determined on the basis of an individual factor (IF) and a stress index (SI),  
IF = WF + AF + TF,  
SI = Sum of {PATF × TIF × TTF} for each possible PATF/TIF combination,  
and the dosage increases as each of IF and SI increases;  
10 wherein  
WF is the weight factor which increases with increasing weight of the individual,  
AF is the age factor which increases with increasing age of the individual,  
TF is the training factor which increases as the extent of past physical training of the individual decreases,  
15 PATF is a physical activity type factor of a current and/or future physical activity of the individual and PATF increases as the physical exertion required to perform the corresponding physical activity increases,  
TIF is the training intensity factor, where TIF increases as the intensity of the individual's performance of a corresponding physical activity increases, and  
20 TTF is a training time factor for a corresponding PATF/TIF combination, where TTF increases as the time spent by the individual performing a corresponding physical activity increases.
24. An anti-oxidant mixture comprising the following amounts of the following  
25 constituents: between 100c and 200c mg of bioflavonoids from pine bark, between 50c and 100c mg of Alpha lipoic acid, between 50c and 100c mg of Vitamin C and/or its derivatives, and between 100c and 200c mg of Vitamin E and/or its derivatives, wherein c is a positive number.
- 30 25. An anti-oxidant mixture according to claim 24, wherein said anti-oxidant mixture comprises the following amounts of the following constituents: 150c mg of

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bioflavonoids from pine bark, 100c mg of Alpha lipoic acid, 100c mg of a Vitamin C ester, and 100c mg of Vitamin E as d-alpha – tocopherol acid succinate, c being a positive number.

- 5    26.    An anti-oxidant mixture according to claim 24, wherein said anti-oxidant mixture comprises the following amounts of the following constituents: 150c mg of bioflavonoids from pine bark, 50c mg of Alpha lipoic acid, 100c mg of a Vitamin C ester, and 150c mg of Vitamin E as d-alpha – tocopherol acid succinate, c being a positive number.
- 10    27.    An anti-oxidant mixture according to any one of claims 24 to 26, wherein the mixture is presented in the form of a capsule.
- 15    28.    An anti-oxidant mixture according to any one of claims 24 to 27, wherein c=1.

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU01/00597

<b>A. CLASSIFICATION OF SUBJECT MATTER</b>		
Int. Cl. <sup>7</sup> : A61K 31/355, 31/375, 31/385, 31/7048, 35/78, A61P 3/02		
According to International Patent Classification (IPC) or to both national classification and IPC		
<b>B. FIELDS SEARCHED</b>		
Minimum documentation searched (classification system followed by classification symbols)		
Refer Electronic data base consulted below		
Documentation searched other than minimum documentation to the extent that such documents are included in the fields searched		
Electronic data base consulted during the international search (name of data base and, where practicable, search terms used)		
DWPI, MEDLINE, CAPLUS: & keywords antioxidant+, anti oxidant+, vitamin c, ascorbic, vitamin e, tocopherol, lipoic, alphalipoic, thioctic, bioflavonoid+, proanthocyanidin+, pine bark, pinus radiata, vitamin p, hesperidin, dose, dosage, train+, exercise, athlet+, physical activitt, sport+		
<b>C. DOCUMENTS CONSIDERED TO BE RELEVANT</b>		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
X	US5972993A (Ptchelintsev) 26 October 1999 Tables, Examples, Claim 17 "ascorbic acid"	24-28
P,X	US6103756A (Gorsek) 15 August 2000 Claims, Table 1	24-28
X	US5817630A (Hofmann et al.) 6 October 1998 Column 3 lines 16-22, Example 1, claims	24-28
<input checked="" type="checkbox"/> Further documents are listed in the continuation of Box C <input checked="" type="checkbox"/> See patent family annex		
* Special categories of cited documents: "A" document defining the general state of the art which is not considered to be of particular relevance "E" earlier application or patent but published on or after the international filing date "L" document which may throw doubts on priority claim(s) or which is cited to establish the publication date of another citation or other special reason (as specified) "O" document referring to an oral disclosure, use, exhibition or other means "P" document published prior to the international filing date but later than the priority date claimed "T" later document published after the international filing date or priority date and not in conflict with the application but cited to understand the principle or theory underlying the invention "X" document of particular relevance; the claimed invention cannot be considered novel or cannot be considered to involve an inventive step when the document is taken alone "Y" document of particular relevance; the claimed invention cannot be considered to involve an inventive step when the document is combined with one or more other such documents, such combination being obvious to a person skilled in the art "&" document member of the same patent family		
Date of the actual completion of the international search		Date of mailing of the international search report
10 July 2001		16 July 2001
Name and mailing address of the ISA/AU		Authorized officer
AUSTRALIAN PATENT OFFICE PO BOX 200, WODEN ACT 2606, AUSTRALIA E-mail address: pct@ipaustalia.gov.au Facsimile No. (02) 6285 3929		TERRY SUMMERS Telephone No : (02) 6283 3126

## INTERNATIONAL SEARCH REPORT

International application No.

PCT/AU01/00597

C (Continuation). DOCUMENTS CONSIDERED TO BE RELEVANT		
Category*	Citation of document, with indication, where appropriate, of the relevant passages	Relevant to claim No.
P,X	EP1072265A1 (MEDIS Srl Medical Infusion systems) 31 January 2001 Example VI, paragraph [0016]	24-28
P,X	WO0122958A2 (AVANSIS LIMITED) 5 April 2001 Page 5 line 11- page 6 line12, page 7 line 20- page 8 line 30, Example 1	24-28
Y	Enzogenol antioxidant ACE + selenium product description [retrieved on 5 July 2001] Retrieved from the Internet <URL: <a href="http://www.expressgroup.co.nz/shop/p_detail.asp?code=ENZA&amp;Group=27">http://www.expressgroup.co.nz/shop/p_detail.asp?code=ENZA&amp;Group=27</a> Ingredients, General	24-28
A	Medline Abstract Accession No. PMID 9571703, Kanter M, Free radicals, exercise and antioxidant supplementation, <i>Proc Nutr Soc</i> , February 1998, 57(1), 9-13 Entire abstract	1-23
A	Medline Abstract Accession No. PMID 1897277, Gerster H, Function of vitamin E in physical exercise: a review, <i>Z Ernahrungswiss</i> , June 1991, 30(2), 89-97 Entire abstract	1-23
Y	Adams A K <i>et al.</i> , Antioxidant vitamins and the prevention of coronary heart disease, <i>American Family Physician</i> , 1 September 1999, [retrieved on 3 July 2001] Retrieved from the Internet <URL: <a href="http://www.aafp.org/afp/990901ap/895.html">http://www.aafp.org/afp/990901ap/895.html</a>	24-28
A	Entire article	1-23
Y	Albrecht, Frances, The new generation of antioxidants, <i>Delicious-online</i> , March 1997 [retrieved on 5 July 2001] Retrieved from the Internet <URL: <a href="http://www.healthwell.com/delicious-online/d_backs/Mar_97/nutrition_advisor.cfm">http://www.healthwell.com/delicious-online/d_backs/Mar_97/nutrition_advisor.cfm</a>	24-28
A	Entire article, alpha-lipoic acid	1-23

**INTERNATIONAL SEARCH REPORT**  
Information on patent family members

International application No.  
**PCT/AU01/00597**

This Annex lists the known "A" publication level patent family members relating to the patent documents cited in the above-mentioned international search report. The Australian Patent Office is in no way liable for these particulars which are merely given for the purpose of information.

Patent Document Cited in Search Report			Patent Family Member	
US	5972993	NONE		
US	6103756	NONE		
US	5817630	CA	2200501	
EP	1072265	EP	1074254	
WO	200122958	NONE		
END OF ANNEX				